

manner using an aqueous solution of unmodified gold nanoparticles. The reversible changes seen in Figure 8A are not observed.

Figures 9A-B: Transmission Electron Microscope (TEM) images. Figure 9A is a TEM image of aggregated gold nanoparticles held together by hybridization of the oligonucleotides on the gold nanoparticles with linking oligonucleotides. Figure 9B is a TEM image of a two-dimensional aggregate showing the ordering of the linked nanoparticles.

Figure 10: Schematic diagram illustrating the formation of thermally-stable triple-stranded oligonucleotide connectors between nanoparticles having the pyrimidine:purine:pyrimidine motif. Such triple-stranded connectors are stiffer than double-stranded connectors. In Figure 10, one nanoparticle has an oligonucleotide attached to it which is composed of all purines, and the other nanoparticle has an oligonucleotide attached to it which is composed of all pyrimidines. The third oligonucleotide for forming the triple-stranded connector (not attached to a nanoparticle) is composed of pyrimidines.

Figure 11: Schematic diagram illustrating the formation of nanoparticle aggregates by combining nanoparticles having complementary oligonucleotides attached to them, the nanoparticles being held together in the aggregates as a result of the hybridization of the complementary oligonucleotides. In Figure 11, the circles represent the nanoparticles, the formulas are oligonucleotide sequences, and s is the thio-alkyl linker. The multiple oligonucleotides on the two types of nanoparticles can hybridize to each other, leading to the formation of an aggregate structure.

Figures 12A-F: Schematic diagrams illustrating systems for detecting nucleic acid using nanoparticles having oligonucleotides attached thereto. Oligonucleotide-nanoparticle conjugates 1 and 2 and single-stranded oligonucleotide targets 3, 4, 5, 6 and 7 are illustrated. The circles represent the nanoparticles, the formulas are oligonucleotide sequences, and the dotted and dashed lines represent connecting links of nucleotide.

Figures 13A-B: Schematic diagrams illustrating systems for detecting DNA (analyte DNA) using nanoparticles and a transparent substrate.

Figures 14A-B: Figure 14A is a graph of absorbance versus wavelength in nm showing changes in absorbance when gold nanoparticles having oligonucleotides attached thereto (one population of which is in solution and one population of which is attached to a transparent substrate as illustrated in Figure 13B) aggregate due to hybridization with linking oligonucleotides. Figure 14B a graph of change in absorbance for the hybridized system referred to in Figure 14A as the temperature is increased (melted).

Figures 15A-G: Schematic diagrams illustrating systems for detecting nucleic acid using nanoparticles having oligonucleotides attached thereto. Oligonucleotide-nanoparticle conjugates 1 and 2 and single-stranded oligonucleotide targets 3, 4, 5, 6, 7 and 8 are illustrated. The circles represent the nanoparticles, the formulas are oligonucleotide sequences, and S represents the thio-alkyl linker.

Figures 16A-C: Schematic diagrams illustrating systems for detecting nucleic acid using nanoparticles having oligonucleotides attached thereto. Oligonucleotide-nanoparticle conjugates 1 and 2, single-stranded oligonucleotide targets of different lengths, and filler oligonucleotides of different lengths are illustrated. The circles represent the nanoparticles, the formulas are oligonucleotide sequences, and S represents the thio-alkyl linker.

Figures 17A-E: Schematic diagrams illustrating nanoparticle-oligonucleotide conjugates and systems for detecting nucleic acid using nanoparticles having oligonucleotides attached thereto. The circles represent the nanoparticles, the straight lines represent oligonucleotide chains (bases not shown), two closely-spaced parallel lines represent duplex segments, and the small letters indicate specific nucleotide sequences (a is complementary to a', b is complementary to b', etc.).

Figure 18: Schematic diagram illustrating a system for detecting nucleic acid using liposomes (large double circle), nanoparticles (small open circles) and a transparent substrate. The filled-in squares represent cholesteryl groups, the squiggles represent oligonucleotides, and the ladders represent double-stranded (hybridized) oligonucleotides.

Figures 19A-B: Figure 19A is a graph of absorbance versus wavelength in nm showing changes in absorbance when gold nanoparticle-oligonucleotide conjugates assemble

in multiple layers on a transparent substrate as illustrated in Figure 13A. Figure 19B is a graph of change in absorbance for the hybridized system referred to in Figure 19A as the temperature is increased (melted).

Figures 20A-B: Illustrations of schemes using fluorescent-labeled oligonucleotides attached to metallic or semiconductor quenching nanoparticles (Figure 20A) or to non-metallic, non-semiconductor particles (Figure 20B).

Figure 21: Schematic diagram illustrating a system for detecting target nucleic acid using gold nanoparticles having oligonucleotides attached thereto and latex microspheres having fluorescently-labeled oligonucleotides attached thereto. The small, closed, dark circles represent the nanoparticles, the large, open circles represent the latex microspheres, and the large oval represents a microporous membrane.

Figure 22: Schematic diagram illustrating a system for detecting target nucleic acid using two types of fluorescently-labeled oligonucleotide-nanoparticle conjugates. The closed circles represent the nanoparticles, and the large oval represents a microporous membrane.

Figure 23: Sequences of materials utilized in an assay for Anthrax Protective Antigen (see Example 12).

Figure 24: Schematic diagram illustrating a system for detecting target nucleic acid using a "satellite probe" which comprises magnetic nanoparticles (dark spheres) having oligonucleotides (straight lines) attached to them, probe oligonucleotides (straight lines) hybridized to the oligonucleotides attached to the nanoparticles, the probe oligonucleotides being labeled with a reporter group (open rectangular box). A, B, C, A', B', and C' represent specific nucleotide sequences, with A, B and C being complementary to A', B' and C', respectively.

Figures 25A-B: Schematic diagrams illustrating systems for detecting DNA using nanoparticles and a transparent substrate. In these figures, a, b and c refer to different oligonucleotide sequences, and a', b' and c' refer to oligonucleotide sequences complementary to a, b and c, respectively.